REMARKS

Claims 67-83, 85-96, and 108 are presently under examination in the case. Claims 97-107 are withdrawn. Claims 1-66 and 84 stand cancelled. Claims 67, 69, 73, 74, and 81 are newly cancelled without prejudice. Claims 68, 70, and 90 are hereby amended. Claims 109-111 have been added. Upon entry of the amendment, claims 68, 70-72, 75-80, 82-96, and 108-111 will be pending and under examination.

Withdrawn claims 97, 98, 99, 101, 105, and 107 also have been amended to correct informalities and render the subject matter thereof commensurate with the claims currently under examination. Claims 112-114 have been added and withdrawn. The right to rejoinder of the withdrawn process claims is requested.

No new matter is presented by virtue of the within amendments. For example, support for the amendment to claims 68 and 70 can be found throughout the specification, in particular at page 6, lines 29-31 (paragraph 28). The amendment to claim 90 is submitted merely to correct a typographical error. New claims 109-111 have been added; support therefore can be found throughout the application, see, for example, page 4, lines 26-31 (paragraph 14); page 10, lines 10-11 (paragraph 42); and page 11, lines 33-34 (paragraph 49). Newly added withdrawn claims 112-114 are supported, for example in withdrawn claim 97.

Referring now to the Office Action, claims 67-96 stand rejected on the grounds of nonstatutory obviousnesss-type double patenting over claims 1-3, 8-17, 22-29 and 34-37 of US Patent No. 6,713,089. The opportunity to file a terminal disclaimer to overcome the rejection is acknowledged.

The remaining rejections are discussed in combination for the sake of brevity.

Claims 67-72, 74-78 and 81-83 and 85-95 stand rejected under 35 USC §103(a) over Penkler et al., US Patent No. 5,854,226 (the ‘226 patent).

Claim 73 stands rejected under 35 USC §103(a) over the '226 patent and further in view of Penkler, WO 95/32737 (the '737 publication).

Claims 79-80 and 96 are rejected under 35 USC §103(a) over the '226 patent and further in view of Sallman et al., US Patent No. 4,296,128 (the '128 patent).

Each of the rejections is traversed. The references cited, even in the stated combinations, do not teach or suggest the features of the claimed invention in any manner sufficient to sustain the rejections.

For instance, independent claims 68 and 70 each recite the following feature:

> …the composition being in the form of a particulate composition or being based on a particulate composition; wherein the quick release pharmaceutical composition contains the active substance in contact with an alkaline substance…

The Office Action states that the '226 patent teaches a pharmaceutical composition for oral administration comprising an inclusion complex of a non-steroidal anti-inflammatory drug (NSAID), an alkaline earth metal bicarbonate, and further active ingredients (at page 8).

The instant claims as set forth above require that the active substance be in contact with the alkaline substance. This is clearly distinct from the inclusion complex containing the active ingredient taught by the cited reference in which the active agent cannot contact the alkaline substance. It would be understood by one skilled in the art that such inclusion complexes imply that the NSAID is enclosed in the cyclodextrin cavity and not available for interaction with other substances in subsequent steps of the method. Such distinctions were noted (and deemed persuasive) during prosecution of the parent application, which has since granted as US Patent No. 6,713,089. For that reason alone, the claims of the present application are not obvious in view of the '226 patent.

It is furthermore believed that such a modification to the beta-cyclodextrin inclusion complex to contact the NSAID directly with an alkaline substance would not be possible. This is because the internal surface of a beta-cyclodextrin molecule is hydrophobic, and therefore suited for interacting with the hydrophobic surface of the lornoxicam molecule. However sodium bicarbonate is a hydrophilic molecule, and does not have hydrophobic properties. One skilled in the art would not consider trying to insert a combination of the hydrophilic sodium bicarbonate molecule and the hydrophobic lornoxicam into the hydrophobic interior of a beta-cyclodextrin molecule. There would be no reasonable expectation of success due to the different chemical natures of lornoxicam and sodium bicarbonate.

Moreover, as the goal of the '226 invention is to provide an “alkaline diffusion layer around the composition in the gastrointestinal tract” (col 2, lines 29-30), one would not be motivated to modify the teachings of the ‘226 patent to contact the alkaline substance directly with the NSAID in an inclusion complex.

The present claims require that

> …the composition, when tested in accordance with the dissolution method I defined herein employing 0.07 N hydrochloric acid as dissolution medium, releases at least 50% w/w of the active substance within the first 20 minutes of the test.

Applicant submits that based on the teachings of the instant application, one would not expect the compositions of the ‘226 patent to have the necessary dissolution properties as required by the present claims. As noted in the Office Action, the 30 mesh used in the ‘226 patent would be equivalent to a 600 µM sieve. The instant application demonstrates that the use of smaller sieve sizes results in faster rates of dissolution. For example, in Examples 6 and 9 in the instant application, the release rate from the composition depends on the particle size of the final particulate composition comprising the active ingredient in contact with the alkaline substance after

being contacted with an aqueous solution and dried. Example 6 demonstrates the effect of increasing the particle size of the particulate composition. Even a slight change in the particle size below or above 212 μM markedly effects the dissolution rate. For example, a tablet composition based on a particulate composition with a mean particle size less than 212 μM results in 93.1% dissolved NSAID after 20 minutes using the dissolution testing method. Conversely, a tablet based on particulate composition with a mean particle size above 212 μM results in 85.4% dissolved NSAID after 20 minutes using the dissolution testing method. Thus, upon decreasing the mean particle size of the particulate composition, the dissolution rate becomes markedly faster. From Example 9, it can be seen that in the case wherein about 60% of the particulate composition has a particle size less than 180 μM, the amount of dissolved NSAID after 20 minutes using the dissolution testing method is no more than 65.8%. Therefore, it would be expected that the compositions of the '226 patent having much larger particle sizes would not likely have the required dissolution profile to meet the limitations of the instant claims. In support of these arguments, attention is directed to the parent application for the Rule 132 Declaration of Poul E. Bertelsen.

The Office Action goes on to suggest that the selection of a smaller mesh would have been obvious to one of skill in the art. Applicant respectfully disagrees. Using the testing method of the '226 patent, one would expect that the composition has a satisfactory dissolution rate based on the testing performed in the '226 patent which is stated to have resulted in 80% dissolution at 30 minutes at pH ~6.5 at 37 ^{o}C. These conditions are similar to those in the intestine where absorption of the composition of the '226 patent is expected to at least partially occur (col 3, line 57). The dissolution properties of a composition at pH 6.5 cannot predict the dissolution properties of a composition in 0.07 N HCl as claimed.

Moreover, the composition of the '226 patent was stated to have improved absorption properties as compared to commercially available tablets containing the same active ingredient (col 3, lines 49-50). Therefore, one skilled in the art would not

have been motivated to modify the method of tablet preparation or dissolution testing based on the favorable results presented in the '226 patent.

As independent claims 68 and 70 are not obvious in view of the '226 patent, the claims dependent thereon also are not obvious in view of the '226 patent. Withdrawal of the rejection is respectfully requested.

Claim 73 stands rejected for alleged obviousness over the '226 patent and further in view of the '737 publication. Due to the amendment of claims 68 and 70, and without acquiescing to the grounds for rejection, claim 73 has been cancelled to expedite allowance of the application, thus rendering the rejection is moot.

Claims 79-80 and 96 stand rejected for alleged obviousness over the '226 patent and further in view of the '128 patent.

The '128 patent does not remedy the deficiencies of the '226 patent. The documents, even in combination, fail to teach or suggest the feature of the invention wherein the active substance is in contact with the alkaline substance. As discussed above, the '226 patent requires an inclusion complex in which the active agent is contained, preventing it from contacting the alkaline agent. The '128 patent provides no suggestion which would cause one skilled in the art to modify the teachings of the '226 patent to contact the active agent with the alkaline agent as claimed presently. The rejection is therefore properly withdrawn.

Accordingly, each of the §103(a) rejections is properly withdrawn. For example, it is well-known that to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference(s) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the

reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaec*k, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143.

There is no suggestion or motivation, either in the reference(s) themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the cited reference(s) to make the claimed invention, nor is there a reasonable expectation of success.

In view of the above amendments and remarks, Applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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